

Use of isolated trout hepatocytes to predict measured hepatic clearance and whole-animal bioconcentration factors for six polyaromatic hydrocarbons.

K.A. Fay, P.N. Fitzsimmons, A.D. Hoffman, J.W. Nichols

U.S. EPA, ORD, NHEERL, Mid-Continent Ecology Division, Duluth, MN USA

Contact: Fay.Kellie@epa.gov

Hepatic metabolism is an important determinant of chemical bioaccumulation in fish. Consequently, measured in vitro hepatic metabolism may improve model predictions of bioaccumulation. In this study, fresh and cryopreserved trout hepatocytes were used to measure in vitro intrinsic clearance ($CL_{in\ vitro,int}$) of six polyaromatic hydrocarbons. These $CL_{in\ vitro,int}$ values were then extrapolated to the intact organ and compared to measured levels of clearance (CL_H) by isolated perfused trout livers. To facilitate these comparisons, hepatocellularity scaling factors were determined for male and female trout. In addition, solid phase microextraction (SPME) methods were employed to determine unbound chemical concentrations in the isolated liver preparation. Generally, the hepatocytes performed well in predicting CL_H rates exhibited by perfused livers. Although hepatocellularity values were higher for female trout than for males, predicted CL_H values for the six compounds did not differ substantially. Finally, CL_H values determined using both hepatocytes and isolated perfused livers were extrapolated to the whole animal and incorporated into a one-compartment bioconcentration model. Model-predicted bioconcentration factors (BCF) were then compared to measured values for strain- and temperature-matched trout. Preliminary results suggest that predicted BCF values are within the range of observed values.